SEDATION OF PEDIATRIC PATIENTS IN MAGNETIC RESONANCE IMAGING

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SEDATION OF PEDIATRIC PATIENTS IN MAGNETIC RESONANCE IMAGING

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PREFACE

This research was conducted to evaluate the safety and efficacy of a pediatric sedation regimen for magnetic resonance imaging at a midwest medical facility. It was designed to support the use of pediatric sedation outside of the operating room.

DEDICATION

To the most High who promised success in *Isaiah* 40:31, I dedicate this thesis work to you Lord. To my family, whose love and support help make this journey possible. I love you, Mike, with all of my heart. Thank you, Mom and Dad, for building the foundation of hard work and perseverance within me. Hambee, Lippess, and Delaine, you were the wind beneath my wings!

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ABSTRACT

Sedation of the pediatric patient is a process carefully planned by the anesthesia provider. Providing anesthesia to pediatric patients requiring a magnetic resonance imaging presents challenges to the caregiver. The effect of the medication on the pediatric patient's hemodynamic and respiratory system is of most concern to the anesthetist. At Wright-Patterson Air Force Base Medical Center (WPAFBMC), a combined intramuscular administration of ketamine, midazolam and atropine is used to gain cooperation and immobility of pediatric patients during MRI scanning while keeping the patient hemodynamically stable. The purpose of this study was to explore this drug combination administered at WPAFBMC for pediatric sedation and determine if it is safe and effective for pediatric patients undergoing MRI scans. A sample of 51 pediatric charts was reviewed retrospectively. Heart rate, respirations and pulse oximetry were evaluated before and after the combined intramuscular drug combination was given. The use of a propofol infusion for additional sedation was also recorded. The results of this study indicate that this regimen is a safe and effective one.

(1) Hemodynamics and respirations remained unchanged after the drug combination was administered.

(2) A propofal infusion was required with all scans.

The results of the study support the pediatric sedation regimen at Wright Patterson Air Force Base as a safe one. An ongoing need for hemodynamic and respiratory monitoring will continue to help provide a safe and effective plan of care by the anesthesia provider.

Key Words: **sedation** **pediatrics** **magnetic resonance imaging** **atropine** **midazolam** **versed**

CHAPTER I: INTRODUCTION

Background

Magnetic resonance imaging (MRI), a non-invasive radiographic test, is used to aid the diagnosis of diseases and abnormalities. It requires a cooperative and immobile patient for approximately 30-90 minutes (Tobin, Spurrier, & Wetzel, 1992). Immobilizing a child for this length of time is a challenge. History has shown that most young children are unable to remain motionless for the extended length of time necessary to perform a MRI examination without sedation (Bisset & Ball, 1991). Providing the sedation is the responsibility of the anesthesia provider.

Gaining intravenous access by venipuncture is the first priority of the anesthesia provider. The anxiety and fear of the needle perceived by the pediatric patient may result in an uncooperative child and a dissatisfied radiologist. The challenge to anesthesia providers is keeping the child immobilized during the MRI scan without compromising respiratory or hemodynamic status. A sedation regimen that is planned must provide hemodynamic and respiratory stability for the patient.

Planning pediatric sedation

Sedation of the pediatric patient is a process carefully planned by the anesthesia provider. Achieving cooperation and immobility of the patient are the main concerns for the radiologist while performing the MRI scan. Any sudden movements by the pediatric patient can result in an inconclusive scan. Hubbard, Markowitz, Kimmel, Kroger, and Bartko (1992) demonstrated that the failure of sedation to enable completion of an examination is more frequent with MRI scan than with other imaging modalities. A study by Slovis and associates (1993) concluded that after repeated failed MRI scans, it is advisable to use the most effective drug regimen with the fewest side effects to provide sedation for pediatric patients. The problem for the anesthesia provider is developing a sedation regimen that renders immobility of the pediatric patient without compromising their respiratory or hemodynamic status. At a midwest medical facility near Dayton, Ohio, such a regimen has been developed and implemented.

A midwest medical facility regimen

At this midwest medical facility, the use of an intramuscular combination of ketamine, midazolam, and atropine with a propofol infusion is used for pediatric sedation for magnetic resonance imaging (Worrell & McCune, 1993). First used as an intravenous sedation, the ketamine, midazolam and atropine combination is now given intramuscularly by a certified registered nurse anesthetist (CRNA). Coordination of the plan of sedation involves the anesthesia provider, the radiologist and the parent of the infant or child. Together they ensure an effective and safe sedation regimen for the patient. Pediatric sedation for MRI scans is very important as these scans are used more frequently for disease diagnosis in these patients.

The dramatic growth in the volume and types of interventional radiology procedures performed during the past five to ten years has been documented by many institutions (Mueller, Wittenberg, Kaufman & Lee, 1997). The success of MRI scans in further diagnosing diseases has lead to its increased use with patients of all ages. Along with this growth, there has been an increase in the demand for, and use of, intravenous analgesia or conscious sedation for these types of procedures. Trained individuals with knowledge of pediatrics and the effects of sedating medications on this patient population are essential in the MRI setting.

Specifically trained individuals, (CRNAs or anesthesiologists), at each MRI site should determine the type of monitoring and sedation to be utilized with pediatric patients (Shellock, 1995). Nurse anesthetists, along with the anesthesiologist, share that responsibility at the medical facility. This facility instituted the intramuscular regimen previously described with the expert knowledge of a certified nurse anesthetist who not only recognized the need for effective and safe pediatric sedation, but also addressed the need of the child's emotional and physiological stress unique to pediatric patients (Worrell & McCune, 1993).

Sedation of the pediatric patient can be a tedious process for the anesthesia provider. Immobility of the patient is the main concern for the radiologist while performing the MRI scan. The hemodynamic and respiratory status of the pediatric patient is the main concern for the anesthesia provider. At the facility, an experienced CRNA who is knowledgeable in the side effects of ketamine, midazolam and atropine with pediatric patients, developed her own formula for an intramuscular administration of a midazolam, ketamine, and atropine mixture with a propofol infusion for continued sedation.

Medications

Ketamine is often a drug chosen by anesthetists because it provides anesthesia, amnesia, and analgesia when administered (Stoelting & Miller, 1994). This drug's peak affects can be seen within two to four minutes after the drug is administered. A patient can be awake but calm depending on the amount of drug given. However, side effects of dissociative behavior and increased airway secretions could endanger the patient. The administration of an anticholinergic like atropine to decrease secretions is advisable since it decreases the side effect of ketamine (Worrell & McCune, 1993). The CRNA at the midwest medical facility initially utilized a sedation regimen initiated by her colleagues. This regimen combined ketamine and midazolam given intravenously to pediatric patients prior to MRI scans.

Midazolam is a benzodiazepam, exerting most of its effects on the nerve endings of the brain and spinal cord (Stoelting & Miller, 1994). Adverse effects such as respiratory depression and a decrease in blood pressure can occur. The immature nervous system of pediatric patients makes them vulnerable to these effects. Midazolam, given in combination with ketamine, decreases the dissociative side effects of ketamine without depressing the patient's respirations. MRI scanning times vary, frequently requiring longer sedation. Propofol, an adjunctive drug to the regimen, is often used to provide additional sedation for longer cases. It was chosen because of its rapid onset of effect and recovery time, and antiemetic effect (Levati, et al., 1996). Propofol has a peak onset of action within 30 to 60 seconds, a fact which makes it ideal for aiding in sedating pediatric patients. This drug combination of ketamine, atropine, and midazolam given intramuscularly, with a propofol infusion, provides a safe and effective sedation regimen that makes the MRI scan a success and less stressful to the pediatric patient. The various effects of these medications on the hemodynamics of the patient requires stringent attention throughout the scanning process. Monitoring the effects of the sedation requires the use of safe equipment and is the responsibility of the anesthesia provider.

<u>Monitoring equipment</u>

Monitoring the pediatric patient during sedation for MRIs is essential to anticipate potential side effects of sedative drugs (http://www.springnet.com/ce/ce/ce966tx.htm).

Monitoring equipment in close proximity to the magnet may malfunction because of the strength of the high magnetic field (Tobin et al., 1992). Visual aids such as cameras, pulse oximetry, and non-invasive blood pressure cuffs allow monitoring necessary to evaluate the respiratory and hemodynamic status of the patient (Worrell & McCune, 1993).

At the midwest medical facility, the nurse anesthetist coordinates her equipment needs with the radiologist to ensure the safety of the patient, anesthetist and radiology personnel. Shellock, Lipczak, & Kanal (1995) report that several hazards are associated with the performance of patient monitoring during MRI examinations. Physiologic monitors that contain ferromagnetic components like transformers and outer castings can be strongly attracted by the static field used by the MRI system. The large magnet used for imaging produces the static field. Unlike household magnets, this magnet has a force of attraction so strong that pens and barrettes become missiles in its proximity. In addition for potential damage to the MRI system, this poses a serious hazard to patients and MRI technicians (Holshouser, Hinshow, & Shellock, 1993).

Some electronic monitors produce their own radio frequency pulses and degrade image quality of the MRI image (Jorgensen, Messick, Gray, Nugent & Berquist, 1994). Providing effective sedation decreases incidence of patient immobility, which is the most common cause of degraded image quality. The pharmacological properties of ketamine, midazolam, and atropine provide the sedation levels needed to render the patient immobile, while maintaining hemodynamic and respiratory stability (Worrell & McCune, 1993).

Pharmacology of ketamine.

Ketamine is a phencyclidine derivative that produces a central dissociation between the thalamus and limbic systems (Stoelting, 1987). It is a white, crystalline compound soluble in water and produces a clear, colorless solution when mixed (Young, 1971). Ketamine's lipid solubility, a measure of how effective the drug diffuses to the blood and brain, is 10 times that of thiopental and after intravenous injection, was found to have an onset of 30 to 60 seconds and duration of 10-15 minutes (Loo, Thomas, Tan, Yeo & Sia, 1997). This character of the drug makes it ideal for sedation and rapid recovery. Ketamine causes an increase in heart rate and systemic blood pressure as well as copious amounts of oral secretions. The anticholinergic effects of atropine decrease the production of secretions, which could obstruct the airway.

Emergence is the time of recovery from the effects of a drug. Emergence delirium is an agitated state of recovery from a drug that often requires the use of restraints (Stoelting & Miller, 1994). Emergence delirium occurs more frequently in older children sedated with ketamine alone (Sussman, 1994). However, this same literature shows that occurrences of emergence delirium are greatly decreased when given in combination with midazolam. Emergence is the time of recovery from the affects of a drug. Emergence delirium is an agitated state of recovery from a drug that often requires restraint (Stoelting & Miller, 1994). Emergence occurs more frequently in patients greater than eight years old who have been sedated with ketamine alone (Sussman, 1994). However this same literature shows that events of emergence delirium are greatly decreased when given in combination with midazolam.

Pharmacology of midazolam.

Midazolam is a benzodiazepine, which exerts its pharmacological effects by enhancing the chloride channel gating function of the inhibitory neurotransmitter gamma aminobutyric acid, GABA (Stoelting & Miller, 1994). The majority of benzodiazepine receptors are contained within the cerebral cortex. Like ketamine, midazolam is a highly lipid soluble medication, resulting in rapid entrance into the central nervous system followed by redistribution to inactive tissue sites. The combined use of midazolam and ketamine alone was found to be safe and effective for minor dental procedures (Roelofse, Joubert, & Roelofse, 1996) however excess oral secretions in a supine patient, such as a pediatric on an MRI table, is hazardous. The combined use of ketamine and midazolam can produce increased oral secretions that could block the airway. This risk necessitates the need for an anticholinergic like atropine.

Pharmacology of atropine.

Atropine is an anticholinergic which produces an anti-salivary effect, thereby, decreasing the side effects of ketamine induced increased secretions (Stoelting & Miller, 1994). Anticholinergics also prevent bradycardia, a decrease in heart rate that may occur with the administration of propofol. The combination of midazolam, ketamine and atropine in conjunction with the intravenous infusion of propofol, inhibits the side effects of each drug if individually given.

Pharmacology of propofol.

Propofol is a lipid soluble substituted isopropylphenol that produces rapid induction of anesthesia followed by rapid awakening in four to eight minutes after the infusion is discontinued (Stoelting & Miller, 1994). Propofol is frequently used alone during MRI examinations. According to Levati et al. (1996) during the MRI scan, anesthesia was considered satisfactory when the patient did not move, pulse oximetry and end tidal carbon dioxide levels were maintained in the normal range and blood pressure and respiratory rate were maintained at baseline values. This data is reassuring to the anesthesia provider since propofol is known to depress the blood pressure and ventilation.

Significance of the Problem.

The task of providing effective sedation while maintaining the protection of the pediatric patient's respiratory and hemodynamic status is not a new challenge to anesthesia providers. Vade, Sukhani, Dolenga & Habisohn-Schuck (1995) studied the use of chloral hydrate sedation of children undergoing CT and MRI imaging. They reported that this regimen was effective despite the fact that 20 percent of the children in their study developed respiratory problems. The use of high dose oral chloral hydrate accounted for mild hypoxia in several children in a study by Greenberg, Faerber, Aspinall, & Adams (1993).

Cote (1994) reported that the protective airway reflexes are lost with deep sedation. This situation requires greater vigilance and monitoring in children than in adults. The American Academy of Pediatrics established and implemented guidelines to follow with pediatric sedation. These guidelines include frequency of assessing vital signs and equipment needed for monitoring the sedated pediatric patient. Adherence to these guidelines has accounted for the decreased number of adverse outcomes related to pediatric sedation.

Kennelly, Salitorre, and Barnes (1996) reported that the guidelines established by the American Academy of Pediatrics for monitoring and managing pediatric sedation for diagnostic and therapeutic procedures were implemented for all sedation performed at Rush Children's Hospital, Chicago, Illinois. After implementation of these guidelines, a demonstrated decrease in adverse reactions was apparent. The personnel responsible for administering and monitoring these sedations were registered nurses trained in pediatric advanced life support. The nurse anesthetist at the facility uses these guidelines and her knowledge of pediatric sedation to provide a safe and efficacious regimen that is one solution to the problem of pediatric sedation for MRI scans.

Problem

Patients must remain immobile for magnetic resonance imaging. The majority of adult patients are able to remain immobile, however, this is very challenging for pediatric patients. Pediatric sedation is necessary to achieve this immobility while maintaining the heart rate, respirations, and pulse oximetry levels at the patient's baseline values.

Purpose

The purpose of this study was to explore the combination sedative of ketamine, midazolam, and atropine administered intramuscularly and determine if it is safe and effective for pediatric patients undergoing magnetic resonance imaging.

Research Questions

1. What effect does a mixture of midazolam, ketamine, and atropine administered intramuscularly have on the pediatric patient's heart rate, respirations, and pulse oximetry readings?
2. Can the intramuscular administration of a combination of ketamine, midazolam, and atropine provide enough sedation for the immobilization required to complete a MRI scan?

Conceptual Framework

This descriptive study was based upon Sister Callista Roy's Adaptation Model (Roy, 1991). According to Roy, nursing is defined as a theoretical system of knowledge, prescribing a process of analysis and action related to the care of the ill or potentially ill person (1991). The nurse anesthetist in this study provides this process through thorough documentation of past medical history and vigilant monitoring throughout the procedure.

Monitoring of the patient's physiological parameters allows the CRNA to assess the patient's ability to adapt to certain stimuli. Based on the patient's adaptation to the stimuli, nursing intervention is initiated. This action is derived from Roy's Adaptation Model, (RAM). The focus of the knowledge for nursing practice is an understanding of the person as an adaptive system (Roy, 1997).

Within the RAM, three stimuli that affect the person's ability to adapt were identified. The first, focal stimulus, is considered as the internal or external stimulus most immediately confronting the person, in the case of this study, intravenous catheter placement for the MRI scan. Based on perception of this stimulus, a response will occur (Munn & Tichy, 1987). The second stimulus identified is the contextual stimulus. This involves all environmental factors that present to the person from within and without the person but which are not the focus of the person's attention, in this case, staying immobile for the MRI scan. The final stimulus is the residual which includes all those stimuli that surround or are within the person that have an unclear effect on the current situation, or more specifically, the disease process.

Together, these stimuli elicit responses to which the patient may or may not be able to adapt. The regulator is the body system which induces physiological responses through neural, chemical, and endocrine processes (Roy, 1991). The regulator in this study would be the hemodynamic or respiratory system, more specifically, heart rate, respirations, and oxygen saturation. The cognator , the body system that elicits responses through perceptual processing and learning, is the pediatric patient. The ability of this patient to process the stimuli from internal and external may affect the adaptation of the patient.

Monitoring of these areas will alert the CRNA to needed intervention to assist the patient to adapt. Taking into account these stimuli and the effect or potential effect they may have on the patient's ability to adapt to them, the CRNA becomes a vital link between the regulator, cognator and perception of the patient (Phillips et al., 1998). This model has been used in previous pediatric studies, for example: care of an eight year old with leukemia (Wright, Holcombe, Foote, & Piazzo, 1993), care given on a neuroscience unit to pediatrics (Frederickson & Williams, 1997), responses to venipuncture (Bournaki, 1997), and adjustment of adolescents with cystic fibrosis (Russell, Reinbold, & Maltby, 1996).

Roy's Adaptation Model is viewed as an excellent model for pediatric nursing research (Betz & Beal, 1996). Roy has even suggested that models such as her own provide a perspective for research, separating the area to be studied and guiding the research questions to be asked (Tolson & McIntosh, 1996). Because the RAM focus is on the dynamics of the adaptive responses to stimuli by the person, this model is most appropriate for this study.

This research design was descriptive and retrospective. The independent variables were the intramuscular administration of ketamine, midazolam, and atropine and the administration of a propofol infusion. The dependent variables were heart rate, respirations, and pulse oximetry reading after drug administration. A t-test analysis was used to compare the difference between the means of the groups. The sample of 51 patients was randomly selected and to reflect the age group of three months to 15 years of age.

Assumptions

1. All patient charts provided accurate baseline vital signs for the required preoperative exam.
2. All the MRI scans required a propofol infusion for prolonging sedation.
3. The regimen for sedation described was utilized by all anesthesia providers involved with MRI scans at the midwest medical facility..
4. All patients received an intramuscular dart combination of ketamine, midazolam and atropine.

Limitations

1. The age spans of the sample ranged from three months to 15 years of age. Different levels of development and coping were expected with age differences.
2. Over the counter medications may be utilized by patients. These medications, such as opiods narcotics, bronchodilators, and barbiturates can provide additional sedation to the patient.
3. This retrospective study was a review of charts. No standardized recordings of vital signs before or after intramuscular medication administration could be applied.

Definitions-Conceptual and Operational

1. Stimulus/stimuli- any internal or external force which produces a positive or negative effect on the individual.
2. Vital signs- the patient's heart rate and respirations per minute.
3. Pulse oximetry saturation- the saturation level of oxygen within the capillary beds of the fingers as measured by infrared waveforms that display numeric readings between the values of 20 through 100 percent.
4. Hemodynamics- that which pertains to the heart rate.
5. Respiratory status- breathing rate per minute.
6. Regulator- the subsystem which induces physiological responses through neural, chemical, and endocrine processes.
7. Cognator- the subsystem which elicits responses through perceptual/information processing, learning, judgement, and emotion processes

Summary

Nursing uses a holistic approach to patient care. Stressors such as venipuncture and IV placement, separation from parent, and unfamiliar sounds can affect the adaptation of pediatric patients to their environment. Magnetic resonance imaging requires the cooperation and immobility of the patient for long periods of time. At the midwest medical facility near Dayton, Ohio, pediatric sedation regimen of a combination of ketamine, midazolam, and atropine administered intramuscular is used. A review of the literature shows safety and efficacy of pharmacologically similar drug combinations. Chapter II will discuss these drugs.

CHAPTER II: LITERATURE REVIEW

Introduction

Pediatric sedation techniques have changed over the years. Twenty years ago male infants receiving a circumcision sucked on bourbon sponges for sedation, today regional anesthetics are used (LtCol J. Ikirt, personal communication, 19 February 1998). Safety of the patient is the paramount concern in all pediatric sedations. According to the guidelines established by the American Academy of Pediatrics, monitoring of the patient should take place before, during and after administration of sedative agents, especially in settings outside the operating room (Committee on Drugs, 1992).

Pediatric sedation for diagnostic and therapeutic procedures, performed outside the operating room setting, have increased dramatically over the last 10 years (Hollman, Elderbrook, & VanDenLangenberg, 1995). Anesthesia providers often administer sedative agents to pediatric patients undergoing diagnostic studies. Some of the responsibilities of the anesthetists lie in their ability to choose a safe and effective drug for the pediatric patient. Within this chapter, a brief review of chloral hydrate's history as a standard in pediatric sedation will be explored. In addition, a review of the literature of various sedative drugs used in pediatrics, such as midazolam, ketamine and propofol, will be discussed. The primary focus will be the drug affect on the patient's heart rate, respiratory rate and oxygen saturation.

Chloral Hydrate History

For many years, different medications have been used in the sedation of pediatric patients. Chloral hydrate is one drug that has gained favor among physicians. Malis and Burton (1997), two pediatric otolaryngologists, described chloral hydrate as the standard agent for pediatric sedation. In their study of its effectiveness for pediatric sedation, they found that oral chloral hydrate was the most frequently used initial medication among 31 radiologists surveyed. Morgan and Mikhail (1996) describe chloral hydrate as a relatively safe and effective drug that could lead to respiratory depression if repeated dosing is required.

Vade, Sukhani, Dolenga, and Habisohn-Schuck (1995), in a study of the use of chloral hydrate for sedation of pediatric patients undergoing MRI scanning, concluded that mild hypoxia (SaO2, 90-95%) seen in the chloral hydrate-only group differed little from the chloral hydrate and hydroxyzine group, at values of 9% and 5%, respectively. These investigators, however, did not explain what constituted a successful MRI scan. Mild hypoxia of the same degree was also seen in a study by Greenberg et al. (1993) while evaluating the safety and efficacy of high dose chloral hydrate sedation for children undergoing MR imaging. The age span of the children in this study are similar to the sample to be evaluated at the midwest medical facility and should provide a good correlation to findings. Frush and Bisset (1997) concluded that chloral hydrate can be used in pediatric sedation, but that the radiologist should balance the pros and the cons, such as gastric irritation with high doses, before administering the drug.

Ineffective amounts of medication are one of the major drawbacks of chloral hydrate. Unlike ketamine, midazolam and atropine, chloral hydrate cannot be given intravenously or intramuscularly. This drawback limits chloral hydrate use to oral administration. When it is given orally, children may vomit. The amount of drug remaining in the stomach may not be effective in providing sedation. Greenberg et al. (1994), radiologists at St. Christopher's Hospital for Children, found that oral thioridazine, an antipsychotic drug with mild antiemetic effects, administered with chloral hydrate, was beneficial in relaxing the difficult-to-sedate child undergoing MRI scanning, however, repeated dosing was required for those patients who vomited. The problem with repeating oral doses is that one cannot be absolutely sure of the amount of medication given.

In a study by Malviya,Voepel-Lewis, and Tate (1997), children sedated with chloral hydrate who experienced inadequate sedation and failed procedure were six years older than those who experienced adequate sedation. These findings reflect the greater effectiveness of chloral hydrate in children under two years of age (Katzung & Trevor, 1996). The willingness of the child to receive chloral hydrate limits its use. Egelhoff, Ball, Koch and Parks (1997) showed that transient respiratory depression (oxygen saturation 10% below baseline) was seen in infants receiving oral chloral hydrate and pentobarbital, however, they do not state what the baseline values of oxygen saturations were. Although response of chloral hydrate may be unpredictable and variable, other drugs such as meperidine and midazolam for sedation of pediatrics are not without fault.

Meperidine and Midazolam

Unlike chloral hydrate, midazolam and meperidine are two drugs that can be administered intravenously and intramuscularly, thus enhancing the complete uptake of the medication by the patient. According to Martyn (1993), the oral route is the easiest and most common way to administer a drug to pediatrics, however, he states that intramuscular injections are beneficial once adequate muscle mass is present. At the University of Southern California School of Dentistry, Malamed, Quinn and Hatch (1989) found that intramuscular (IM) and intravenous (IV) midazolam sedation were more beneficial to their pediatric patients. Of the 31 patients in the study, all ranging in age from 19 months to 11 years, 30 of the cases were successful with one patient needing referral for general anesthesia. Only four patients had pulse oximetry readings fall to 90% or below and heart rates that increased transiently to 140 and above. The investigators failed to report if the unsuccessful case had inadequate muscle mass, a fact that they had reported was the key to intramuscular administration. Terndrup et al. (1991) analyzed the effectiveness of IM meperidine, promethazine and chlorpromazine in the sedation of pediatric emergency department patients. They concluded that this drug combination was effective and safe with only clinically mild but statistically significant changes occurring in respiratory rate, heart rate, systolic blood pressure and Glasgow Coma Scale. Contradictory to this study is the research by Petrack, Marx and Wright (1996) which revealed that intramuscular ketamine has a much faster onset and results in a more rapid discharge from the pediatric emergency department than the results seen with a combination of meperidine, promethazine, and chlorpromazine. Ketamine is one of the drugs in the sedation regimen at the facility which has gained favor among the anesthesia and radiology providers.

Forestner (1987) states that the "pediatric cocktail", which usually consists the same drug combination used by Terndrup and others (1991) is a favorite of radiologists because it produces deep sedation within 30 minutes of IM injection. On the other hand, Moscona, Ramon, Ben-David and Isserts (1995) concluded, while comparing different sedation techniques for outpatient rhinoplasty, that certain limitations and risks lay with the use of standard pediatric lytic cocktails and that newer, short-acting agents such as midazolam, propofol, fentanyl and ketamine should be used instead. This opinion is shared by Taylor, Vine and Hatch (1986) who stated, while evaluating the effectiveness of intramuscular midazolam in small children undergoing diagnostic procedures, that midazolam is an effective premedicant for children when administered intramuscularly, rectally, intranasally or orally. An assumption of the author's proposed study is that all the patients will require a propofol infusion for their MRI scan. The above mentioned studies will provide a background for expected findings. While Sacchetti (1995) concluded that although drugs, such as benzodiazepine and pentobarbital, do nothing to inhibit pain, they are very effective as complete sedative-hypnotics. Drugs such as ketamine provide analgesia as well as sedation for pediatric patients.

Ketamine administration

Ketamine is a phencyclidine analogue that can produce rapid induction of general anesthesia with sedation and analgesia, especially when given intramuscularly (White, 1996). A review of literature shows effectiveness of ketamine administered alone and in combinations with other agents.

Investigating the respiratory interactions of ketamine and morphine, Bourke, Malit, and Smith (1987) found that ketamine alone caused the carbon dioxide response curve to shift to the right, but did not change the slope of the curve, similar to opioids, indicating less of a respiratory effect on the pediatric patient. As stated previously, one of the major side effects of ketamine is emergence delirium which this study did not address. Marx et al. (1997) concluded that a drug combination of ketamine and midazolam given intravenously was more effective at producing sedation with a faster onset and recovery than a combination of midazolam and meperidine. In this study hypoxia (77.8%), hypotension (55.6%), and tachycardia (55.6%) were the most prevalent adverse reactions

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with the meperidine and midazolam combination and clinically insignificant with the ketamine and midazolam combination. This study was more definitive of the criteria for adverse effects of vital signs so one could undoubtedly see the differences between the two drug regimens.

Research continues to show the effectiveness of combining ketamine and midazolam for reducing the delirium emergence and dissociative effects of ketamine when given alone. Anderson and Lerman (1994) and Warner, Cabaret and Velling (1995) reported a decrease of the psychological side effects of ketamine when given orally with midazolam. In similar studies, Louon and Reddy (1994) reported the same results for pediatric patients undergoing computerized axial tomography (CT), who were administered the drugs nasally. As stated before, oral administration of a drug to pediatric patients can not guarantee complete absorption of the medication.

Weksler, Ovadia, Muati, and Stavis (1993) evaluation of nasal ketamine for pediatric premedication identified this route of administration as an alternative for young children aged two to five years of age. Weights and ages of these children were similar to those of the previous studies of Louon and Reddy (1994). Again, emergence delirium has to be expected in a dose of ketamine administered alone and neither study addressed it. Sekerci, Donmez and Okten (1996) evaluated the effects of oral ketamine given to 43 children undergoing ophthalmic surgery and found that 33% of the study group had incidences of nausea and vomiting, but no one displayed emergence delirium. These authors failed to mention an obvious limitation to their study, which is,: with such a high incidence of vomiting, the patients did not experience emergence delirium because they probably did not receive the full, if any part, of the drug dose. However, Donohue and

Dinten (1992) reported that large doses of ketamine and midazolam given orally predisposed children to emergence delirium after radiographic procedures; the children intermittently stared blankly into space and screamed loudly for two minutes before settling down.

The rectal administration of ketamine and midazolam shows a faster onset than other routes of administration except for the intravenous route. Beebe et al. (1992) evaluated the effectiveness of preoperative sedation with rectal midazolam and ketamine given singly or in combinations to young children in need of an intravenous catheter. The study showed that patients separated easily from their parents and remained immobile for IV placement. This study reflects one of the facility's goals for their pediatric sedation regimen and that is to decrease separation anxiety. Oxygen saturations remained above 90% in 92% of all the study groups; the other 8% had transient decreases. In a similar study, Lokken et al. (1994) saw that midazolam alone caused a decrease in the blood oxygen level but when given with ketamine, produced clinically insignificant but statistically significant decreases in the oxygen level of pediatric patients having dental treatment performed. This study further supports the facility's use of a drug combination which includes the ketamine and midazolam. Still, some health care providers find that the rapid onset of intravenous ketamine is more favorable.

Ketamine and Midazolam

The use of ketamine and ketamine midazolam combinations administered intravenously consistently renders faster sedation than other routes. Cotsen, Donaldson, Ueijima, and Morello (1997) studied the efficacy of ketamine sedation in children for interventional radiologic procedures and reported that the average induction time for the

IV sedation route was 45 seconds as compared to 4 minutes for the IM route. While this study helps answer the question whether of a combination of ketamine, midazolam and atropine provides adequate sedation, it does not indicate how much additional time was needed to place the IV. The facility's use of the IM drug dart of ketamine, midazolam and atropine before IV placement provides a cooperative patient and a fast IV placement. Again, this study showed respiratory adverse effects were transient and cardiovascular changes minimal in all the patients. In a two part series evaluating ketamine sedation for pediatric procedures in the emergency room, Green, Nakamura and Johnson (1990) concluded that IM ketamine was sufficient for sedation, but later Green and Johnson (1990) agreed with Hollister and Burn (1974) that intravenous sedation is more desirable for prolonged procedures. Patients at the facility receive a propofol infusion in addition to the drug dart for MRI scans.

During the evaluation of the efficacy and safety of intravenous midazolam and ketamine as sedation for therapeutic and diagnostic procedures for pediatric patients on oncology wards, Parker, Mahan, Gingliano and Parker (1997) showed no serious respiratory and cardiovascular complications. In addition, only 2% of the entire sample experienced transient drops in their oxygen saturations. Likewise, Okamoto, Duperon, and Jedrychowski (1992) chose the same drug combination because of ketamine and midazolam relatively short duration of action on pediatric patients receiving dental examinations. Not only did the children separate from their parents easier, but they also were much more cooperative than prior to receiving the premedication. At the midwest medical facility, anesthesia providers report a fast discharge from the recovery room and attribute it to the short duration of action of ketamine, midazolam and propofol.

Research has shown that few health care providers show a hesitancy of using ketamine unless it is contraindicated. In a review of pediatric conscious sedation, Wertz (1994) and Ramoska (1991) concluded that because of its ability to increase cerebral blood flow and thus intracranial pressure in a compromised cranium, ketamine should not be used in the emergency department with unconfirmed head injuries. The patient population for the proposed study are outpatients or scheduled in patients who have been screened for contraindications for ketamine use. Pruitt, Goldwasser, Sabol and Prstojevich (1995) chose glycopyrrolate, an anticholinergic agent, to combine with ketamine because its quarternary amine structure prevents it from crossing the blood brain barrier and exacerbating the dissociative effects of ketamine thus prolonging recovery. Although a tertiary amine that can cross the blood brain barrier, the midwest facility uses an atropine dose of 0.02mg per kg and its effect on patient will be evaluated in this study. In spite of the faster onset of action when given intravenously, other investigators have found that due to the longer duration of MRI scans, techniques that incorporate the use of narcotics, barbiturates and ketamine, singly or combined, have not provided adequate sedation and that the use of intravenous propofol was more beneficial (Lefever, Potter, & Seeley, 1993).

Propofol

In a study of the pharmacokinetics of propofol, Saint-Maurice, Cockshott, Douglas, Richard and Harmey (1989) reported that the use of propofol produced anesthesia faster because of the larger central compartment in children than in adults and that the rapid metabolism of this agent discontinues its anesthetic effect faster. This characteristic of propofol is confirmed by Burke and Pollock (1994) when explaining that their eight years of using continuous infusion of propofol renders better long term sedation without clinically significant adverse effects. At the facility, propofol is the drug of choice for pediatric patients requiring MRI scans because scans must last longer than the sedative effects of the drug dart used.

The adverse effect causing greatest concern when administering propofol is apnea. Broennele and Cohen (1993), anesthesiologists at Children's Hospital in Philadelphia, Pennsylvania, says that the frequent episodes of apnea produced by continuous propofol infusion makes it unsafe for use with individuals with critical airway and ventilatory issues; infants are an example. In their study, end tidal carbon dioxide and oxygen saturation did not fall below baseline but supplemental oxygen was used. Safety is the primary concern of the anesthesia staff at the facility and, therefore, an evaluation of their pediatric sedation plan is most appropriate to gain further knowledge about the drugs effect on the patient. Whether propofol is considered a primary sedation or secondary method to barbiturates, benzodiazepines and ketamine, it continues to be part of standard pediatric sedation.

Summary

This literature review shows multiple sedative-hypnotics, their different routes of administration and their efficacy and safety for sedation of the pediatric patient. All comment on the effects of various drugs on the pediatric patient's hemodynamic status and respirations but also show that no definite sedation routine for these patients is believed to be better than the other. Ketamine, atropine, midazolam, meperidine and chloral hydrate are sedation agents that each display advantages and disadvantages to their use. The use of propofol has shown favor among physicians for longer MRI scans.

To ensure that anesthesia providers administer safe and efficacious sedation to pediatric patients, further research is necessary. The pediatric sedation regimen at the midwest medical facility will be evaluated for its safety and efficacy of patients receiving MRI scans. In the following chapter, a research plan and methodology to study a pediatric sedation regimen will be described.

APPENDICES

A. Data Collection Tool

B. Data Collection Tool Legend

APPENDIX A

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
1	DX	Ag	Rce	Wt	Bhr	Brr	Bbp	BO2	Med	Ahr	Arr	Abp	AO2	FiO2	TP	PPIM	VPIM	OM		COMMENTS
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APPENDIX B

Legend.

Record Collection Spreadsheet

ID	DX	Ag	Rce	Wt	Bhr	Brr	Bbp	BO2	Med	Ahr	Arr	Abp	AO2	FiO2	TP

Key ID = patient's hospital number
DX = patient's diagnosis, see below
Ag = age in years
Rce = race, see below
Wt = weight in kilograms
Bhr = heart rate per minute before medication
Brr = respiratory rate per minute before medication
Bbp = blood pressure before medication
BO2 = oxygen saturation before medication
Med = ketamine 3mg/kg+midazolam 0.07mg/kg+0.02mg/kg IM, see below
Ahr = heart rate per minute after medication
Arr = respiratory rate per minute after medication
Abp = blood pressure after medication
AO2 = oxygen saturation after medication
FiO2 = percent oxygen used
TP = type of oxygen device used, see below

Coding:

Race
1. Caucasian
2. Black
3. Hispanic
4. Asian
5. Other

Gender
1. Male
2. Female

Medication
1. Given
2. Not given

Diagnosis
1. Oncological
2. Trauma
3. Hematoma

Oxygen type
1. Face mask
2. Nasal cannula
3. Intubated
4. Nothing used

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

May 12, 1998

MEMORANDUM FOR ALESIA D. RICKS, GRADUATE SCHOOL OF NURSING

SUBJECT: IRB Approval of Protocol **T06160-01** for Human Subject Use

Your research protocol entitled ***"Pediatric Sedation in Magnetic Resonance Imaging,"*** was reviewed and approved for execution on 5/8/97 as an **exempt** human subject use study under the provisions of 32 CFR 219.101 (b)(2).

The IRB understands that the study consists of a chart review of 75 children, ages 3 months to 15 years, who have undergone an MRI and required sedation. The study will examine effectiveness of the combination sedative ketamine, midazolam, and atropine administered intramuscularly in producing adequate sedation for the quietude required for MRI scanning.

Please notify this office of any amendments you wish to propose and of any unexpected incidents regarding the protection of human subjects that may occur in the conduct of this project. If you have any questions regarding human volunteers, please call me at 301-295-3303.

Michael J. McCreery

Michael J. McCreery, Ph.D.
LTC, MS, USA
Director, Research Programs and
Executive Secretary, IRB

cc: Director, Grants Administration

DEPARTMENT OF THE AIR FORCE
HEADQUARTERS AIR FORCE MATERIEL COMMAND
WRIGHT-PATTERSON AIR FORCE BASE. OHIO

25 June 1998

MEMORANDUM FOR 74 MDOS/SGOSA
ATTN: CAPT ALESIA RICKS

FROM: 74th MDOS/SGOA
Clinical Investigations
4881 Sugar Maple Drive
Wright-Patterson AFB OH 45433-5300

SUBJECT: Proposed Protocol

1. The protocol you submitted, "Pediatric Sedation in Magnetic Resonance Imaging," was reviewed via expedited review and approved by the Chair of the Institutional Review Board (IRB) of Wright-Patterson Medical Center on 19 June 1998. The Commander of Wright-Patterson Medical Center also reviewed the protocol on 25 June 1998. It was determined to be exempt and has been assigned file number FWP19980025E. You may now begin your study.

2. Progress reports will be due annually. You will receive a reminder 30 days in advance when your report is due. If you complete your study prior to June 1999 a final report may be completed.

3. Any changes to the study must be submitted to the Clinical Ivestigations office for approval prior to initiation.

4. Any unanticipated major adverse reactions or other medical misadventures must be reported immediately to the department chairperson, the Chief of Medical Staff, the Clinical Investigations Coordinator and ultimately the commander IAW AFI 40-403. Such events will also need to be summarized in the subsequent progress report.

5. If you anticipate separating from the Air Force or changing assignments before the protocol is completed, you must notify the Clinical Investigations Office as soon as this is known. You will be required to either formally close the protocol, or to have another investigator take over the study. The latter process requires nomination by the flight commander, submission of a curriculum vitae, and approval by the Institutional Review Board.

6. Please indorse below and return to Clinical Investigations. I hope that your study will prove to be a worthwhile experience for you. Let us know if there is any way we can assist you.

DBachman
DEBBIE BACHMAN
Clinical Investigations Coordinator

1st IND

TO: SGOA/Clinical Investigations

Noted/Acknowledged

Alesia D. Ricks
Principle Investigator

30 Jun 98
Date

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